[2+3]-Cycloadditions of diazoalkanes with imines of hexafluoroacetone and chloral

Mloston, G ; Bodzioch, A ; Cebulska, Z ; Linden, Anthony ; Heimgartner, H

Abstract: The reactions of N-arylimines 1 and 2 of hexafluoroacetone and chloral, respectively, with diazoalkanes at –60°C to room temperature led to the corresponding 4,5-dihydro-1H-[1,2,3]triazoles 4 and 5, respectively, in a regioselective [2+3]-cycloaddition. The structure of one example in each case has been established by X-ray crystallography. The thermal decomposition of these adducts yielded the corresponding aziridines, bearing two trifluoromethyl and one trichloromethyl group, respectively, at C(2).

Polish J. Chem., **81**, xxx–xxx (2007)

[2+3]-Cycloadditions of Diazoalkanes with Imines of Hexafluoroacetone and Chloral*

by G. Mloston[1], A. Bodzioch[1]***, Z. Cebulska[1], A. Linden[2] and H. Heimgartner[2]****

[1]*Section of Heteroorganic Compounds, University of Lodz, Narutowicza 68, PL-90-136 Lodz, Poland*
[2]*Institute of Organic Chemistry, University of Zurich, Winterthurerstrasse190, CH-8057 Zurich, Switzerland*

(Received September 13th, 2006)

The reactions of *N*-arylimines **1** and **2** of hexafluoroacetone and chloral, respectively, with diazoalkanes at –60°C to room temperature led to the corresponding 4,5-dihydro-1*H*-[1,2,3]triazoles **4** and **5**, respectively, in a regioselective [2+3]-cycloaddition. The structure of one example in each case has been established by X-ray crystallography. The thermal decomposition of these adducts yielded the corresponding aziridines, bearing two trifluoromethyl and one trichloromethyl group, respectively, at C(2).

Key words: 1,3-dipolar cycloaddition, imines, 4,5-dihydro-1*H*-[1,2,3]triazoles, aziridines, crystal structure

Aliphatic and aromatic imines are well known as valuable building blocks for the preparation of nitrogen-containing heterocycles. Especially useful are the reactions with diazo compounds to give either 4,5-dihydro-1*H*-1,2,3-triazoles or 3,5-dihydro-4*H*-[1,2,4]triazoles *via* [2+3]-cycloaddition [1,2]. In most cases, the formation of the 1,2,3-triazole derivatives as single or major products was observed (*e.g.* the recently described reactions of diethyl diazomethylphosphonate with aldimines [3]). The importance of these heterocycles is reflected by their biological properties and numerous applications as pharmaceuticals and agrochemicals [4,5]. The opposite regioisomers, *i.e.* 1,2,4-triazole derivatives, are known to eliminate nitrogen under mild conditions yielding aziridines [6]. In some instances, the treatment of the imine with a diazo compound leads directly to aziridines by spontaneous evolution of nitrogen (*e.g.* [3,7])****.

The importance of fluorinated heterocycles is well documented, and the replacement of H-atoms by F-atoms is one of the best known 'bioisosteric' conversions [14,15]. In the

---

* Dedicated to Professor T.M. Krygowski on the occasion of his 70th birthday.

** Authors for correspondence; e-mail: gmloston@uni.lodz.pl

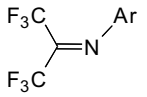
*** Part of the Diploma Thesis of A.B., University of Lodz, 2005.

**** The preferred method for the preparation of aziridines from imines and diazo compounds is the transition-metal catalyzed reaction *via* addition of intermediate carbenoids to the N-atom of the imines to give reactive azomethine ylides. The latter undergo a 1,3-dipolar electrocyclization, which leads to aziridines (see *e.g*. [8–11]). However, a different reaction mechanism was proposed for the iridium-catalyzed aziridination with ethyl diazoacetate [12]. For an example of *asymmetric catalysis* in the synthesis of aziridines, see [13].

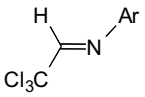
light of the presented reactions of imines, derivatives of hexafluoroacetone are attractive dipholarophiles for reactions with diazo compounds. Astonishingly, very little is reported on such reactions. The first paper describing the reaction of diazomethane with *N*-benzoylhexafluoroacetone imine (2,2,2-trifluoro-1-[(trifluoromethyl)ethylidene]benzamide) reports the formation of 2-phenyl-4,4-bis(trifluoromethyl)-4,5-dihydrooxazole as the sole product [16]. In the reaction of diazoethane with hexafluoroacetone imine, the [2+3]-cycloadduct described as a 1,2,3-triazole derivative was obtained in very low yield [17]. Finally, the third report describes the reaction of diazomethane with a hexafluoroacetone imine bearing a complex phosphorus substituent at the N-atom, yielding again a 1,2,3-triazole derivative [18].

Similarly, reactions of chloral imines (2,2,2-trichloroethylidene amines) with diazo compounds are rarely described and, to the best of our knowledge, are limited to *N*-methoxycarbonyl chloral imine [6,19]. In one case, the reaction with diphenyldiazomethane yielded a 1,2,4-triazole derivative, which easily eliminated nitrogen. The product obtained with ethyl diazoacetate is a formal adduct of the diazo compound to the C=N group *via* formation of a new C,C bond. It is very likely that an initial [2+3]-cycloaddition leads to a 1,2,3-triazole derivative, which subsequently undergoes a ring opening to give the final product.

Due to the general interest on the course of [2+3]-cycloaddition reactions with diazo compounds, we studied their reactions with imines of hexafluoroacetone **1** as well as with a selected chloral imine **2**. The regioselectivity of the reactions and thermal stability of the products were of interest. Additionally, the strongly electron deficient imines **1** and **2** should be tested as potential interceptors of nucleophilic dimethoxycarbene (DMC) in [1+2]-cycloadditions, which would lead directly to the corresponding aziridine derivatives.



1a Ar = 4-MeC_6H_4
b Ar = 2-MeOC_6H_4



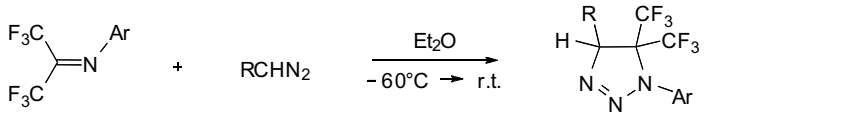
2 Ar = 4-ClC_6H_4

RESULTS AND DISCUSSION

N-Aryl-substituted imines of hexafluoroacetone of type **1** are conveniently available from the hexafluorothioacetone dimer and the respective aniline [20]. In a typical experiment, **1a** was treated with excess of diazomethane or diazoethane (**3a** and **3b**, resp.) at –60 °C and the reaction was completed at room temperature. The ^{1}H-NMR spectrum of the crude mixture of the reaction with **3a** showed that only one product with a characteristic CH_2 absorption at 4.90 ppm was formed. The corre-

sponding signal in the ^{13}C-NMR spectrum appears at 73.1 ppm. These data strongly support the structure of the 1,2,3-triazole derivative **4a** (Scheme 1). According to the reported data, the CH_2 group in the 1,2,4-triazole derivative should absorb at significantly lower field [6,21]. After chromatographic workup, **4a** was obtained as a yellowish oil in 89% yield. Similarly, the reaction of **1b** and diazomethane (**3a**) yielded the crystalline adduct **4b**, in which the corresponding signals of the CH_2 group appeared at 4.85 and 72.1 ppm.

Scheme 1



1a, b **3a** R = H, **b** R = Me

4a R = H, Ar = 4-MeC$_6$H$_4$
b R = H, Ar = 2-MeOC$_6$H$_4$
c R = Me, Ar = 4-MeC$_6$H$_4$
d R = Me, Ar = 2-MeOC$_6$H$_4$

The cycloadducts of **1a** and **1b** with diazoethane (**3b**) were also formed in high yield with complete regioselectivity, as evidenced by the ^{1}H-NMR spectra of the crude mixtures. It is worth mentioning that in the ^{1}H-NMR spectra of **4c** and **4d**, H-C(4) appears as a *qq*-signal with $J_{H,H}$ = 7.5 and $J_{H,F}$ = 1.4 Hz. In turn, a *dq*-signal was observed for Me-C(4) with $J_{H,H}$ = 7.5 and $J_{H,F}$ = 2.1 Hz. The H,F-coupling is the result of a 'through-space' interaction of the respective *cis*-oriented CF_3 group.

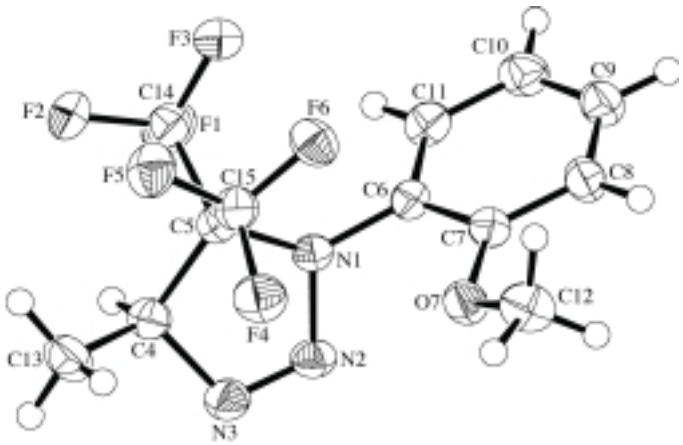


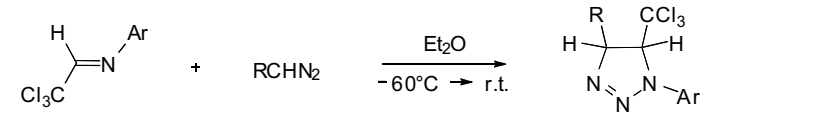
Figure 1. ORTEP-diagram [22] of the molecular structure of **4d** (arbitrary numbering of the atoms; 50% probability ellipsoids).

Finally, the structure of the crystalline product **4d** was established by X-ray crystallography (Figure 1).

In contrast to **3a** and **3b**, which efficiently added to the C,N-double bond of **1**, the attempted reactions with ethyl diazoacetate at room temperature (5 d) or in refluxing toluene (5 h) did not afford any product. Analogously, no formation of [2+3]-cycloadducts was observed when ethyl diazoacetate was replaced by diethyl diazomethylphosphonate.

For comparison, chloral *N*-(4-chlorophenyl)imine (**2**) was reacted with **3a** and **3b**, respectively. Under the reaction conditions applied in the case of **1a** and **1b**, the [2+3]-cycloadducts **5a** and **5b** were obtained as the sole products (Scheme 2). Therefore, the cycloaddition occurred in a completely regioselective manner. The absorption of the CH_2 group of **5a** in the ^{13}C-NMR spectrum (72.1 ppm) supports the structure of the 1,2,3-triazole isomer. Finally, the structure was unambiguously established by X-ray crystallography (Figure 2).

Scheme 2



2 Ar = 4-ClC$_6$H$_4$ **3a**, **b** **5a** R = H, Ar = 4-ClC$_6$H$_4$
b R = Me, Ar = 4-ClC$_6$H$_4$

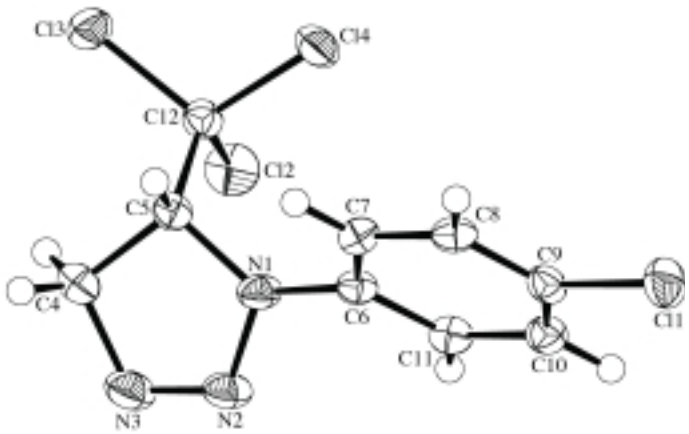
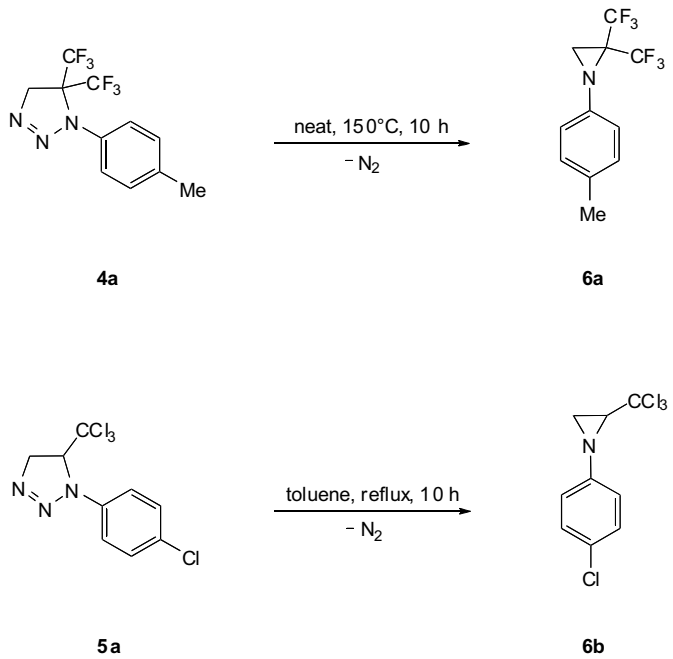


Figure 2. ORTEP-diagram [22] of the molecular structure of **5a** (arbitrary numbering of the atoms; 50% probability ellipsoids).

The thermal elimination of nitrogen from 4,5-dihydro-1,2,3-triazole derivatives is a known method for the preparation of aziridines*. Typical conditions are refluxing toluene or other hydrocarbons [24,25]. In order to test the thermal stability of the products **4,** a solution of **4a** in toluene was heated to reflux for 10 h, but no evolution of nitrogen was observed and the unchanged **4a** was recovered after evaporation of the solvent. After the heating of **4a** without solvent for 10 h to 150°C, an oily material was obtained, which in the ^{1}H-NMR spectrum shows the signals expected for 1-(4-methylphenyl)-2,2-bis(trifluoromethyl)aziridine (**6a**, Scheme 3) (*cf.* [17,26]).

In contrast to **4a,** heating of **5a** in boiling toluene led to the evolution of nitrogen, and after chromatographic separation, a colorless oil was isolated along with small amounts of **2**. The spectroscopic data of the oily material support the structure of the expected 1-(4-chlorophenyl)-2-trichloromethylaziridine (**6b**). This result shows that 1,2,3-triazole derivatives of type **5** extrude nitrogen easier than the corresponding derivatives of type **4**. Enhanced stability of the trifluoromethylated 1,2,3-triazoles **4** can plausibly be explained by the known stabilizing influence of the CF_3-groups, which is of special interest ('magic effect') in the case of small congested rings or linear strained systems (*e.g.* ketene imines) [27].

Scheme 3

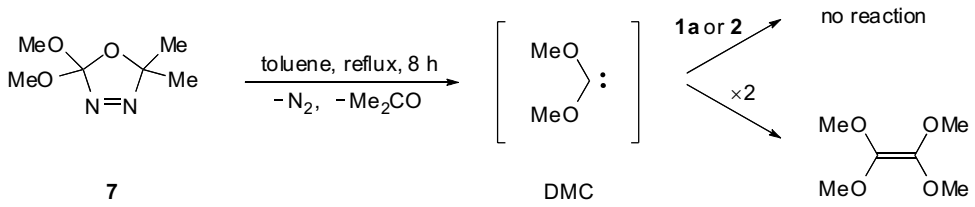


* In many cases, the photolytical conversion is the method of choice [23].

Again, the attempted reaction of **2** with less reactive ethyl diazoacetate both at room temperature (24 h) or in boiling toluene (5 h) failed to give the desired products of the [2+3]-cycloaddition.

As a continuation of the ongoing studies on the reactivity and structure of nucleophilic dimethoxycarbene (DMC) [28], hexafluoroacetone imine **1a** and chloral imine **2** were tested as potential substrates for the synthesis of the corresponding 2,2-dimethoxyaziridines. However, after heating of each of the imines for several hours with 2,5-dihydro-2,2-dimethoxy-5,5-dimethyl-1,3,4-oxadiazole, which is well established as a superior precursor of DMC (toluene, reflux) [29], only unchanged starting materials **1a** and **2** were isolated, and the carbene underwent dimerization to yield tetramethoxyethene as the side product (Scheme 4). Hitherto, no successful transformation of an imine into the corresponding aziridine by a [1+2]-cycloaddition reaction with DMC has been reported.

Scheme 4



In conclusion, the present results show that *N*-aryl-substituted imines of hexafluoroacetone and chloral easily undergo [2+3]-cycloadditions with the reactive di--azomethane and diazoethane. The reactions proceed regioselectively to give the 1,2,3-triazole derivatives. The thermal decomposition of the chloral imine adduct **5a** can be used for the preparation of little know aziridines bearing a CCl_3 group at C(2), which, in turn, are potential candidates for the thermal generation of azomethine ylides.

EXPERIMENTAL

1. General. M.p.'s. were determined on a Boetius apparatus and are not corrected. The IR spectra were registered with a NEXUS FT-IR spectrophotometer (as KBr pellets or as film). The NMR spectra were recorded in $CDCl_3$ solutions on a TESLA BS 687 (^{1}H, 80 MHz; ^{13}C, 20.07 MHz) or a Bruker ARX-300 (^{1}H, 300 MHz; ^{13}C, 75.6 MHz, ^{19}F, 282.3 MHz) instrument. The ^{13}C NMR spectra were recorded by using DEPT registration. The CI-MS and ESI-MS spectra were registered with a Finnigan TSQ-700 triple quadrupole instrument.

2. Starting materials. *Synthesis of hexafluoroacetone imines* **1**. *General procedure*. A mixture of 2,2,4,4-tetrakis(trifluoromethyl)-1,3-dithietane (1.82 g, 0.005 mol) and 0.01 mol of the corresponding amine were dissolved in 10 ml DMF and the solution was stirred magnetically for 1.5 h at room tempera-

ture. The precipitated sulfur was separated by filtration and then 50 ml of water were added to the filtrate. The organic phase was separated, dissolved in 50 ml of Et_2O, washed with water (3×50 ml) and dried over $MgSO_4$. After filtration and evaporation of the solvent, the isolated crude products were purified by distillation.

(4-Methyl-N-*(hexafluoroisopropyliden)aniline)* (**1a**). From 1.07 g (0.01 mmol) of *p*-toluidine. Yield: 0.87 g (73%), pale yellow oil; b.p. 61–63°C/20 Torr ([20]: b.p. 76.5–77°C/30 Torr). IR (KBr): 3035, 2928, 2872, 1653 (C=N), 1577, 1505, 1355, 1254, 1181, 1173, 984, 823. ^{1}H-NMR: 2.35 (*s*, Me); 6.80, 7.20 (*AB*, *J* = 6 Hz, 4 arom. H).

2-Methoxy-N-*(hexafluoroisopropyliden)aniline* (**1b**). From 1.24 g (0.01 mmol) of *o*-anisidine. Yield: 0.32 g (39%), yellow oil; b.p. 70.5–72°C/12 Torr. ^{1}H-NMR: 3.80 (*s*, MeO); 6.70–7.30 (*m*, 4 arom. H).

Synthesis of 4-chloro-N-*(2,2,2-trichloroethylidene)aniline* (**2**). A solution of 4-chloroaniline (1.28 g, 0.01 mol) and chloral (1.61 g, 0.011 mol) in 50 ml of toluene was heated to reflux for 5 h. Non-consumed amine precipitated and was collected by filtration, and the filtrate was evaporated to dryness. The crude solid product was purified by crystallization (hexane). Yield: 1.1 g (43%), colorless solid; m.p. 133–135°C ([30]: b.p. 117–121°C/0.1Torr). IR (KBr): 3089, 3056, 2922, 2856, 1652 (C=N), 1599, 1486, 1458, 1332, 1092, 1012, 947, 883, 833, 787, 746, 684. ^{1}H-NMR: 7.15, 7.40 (*AB*, *J* = 7.6 Hz, 4 arom. H); 7.90 (*s*, N=CH).

2,5-Dihydro-2,2-dimethoxy-5,5-dimethyl-1,3,4-oxadiazole (**7**) was prepared according to a literature protocol [29].

2. Reaction of imines 1 with diazoalkanes 3. *General procedure*. To a solution of the corresponding imine **1** (0.5 mmol) in 3 ml of Et_2O, a three-fold excess of the diazo compound in Et_2O was added at –60°C. After 5 h, the mixture was slowly warmed to room temperature, the solvent was evaporated, and the products were obtained as pure samples. Solids were additionally purified by crystallization from hexane.

*1-(4-Methylphenyl)-5,5-bis(trifluoromethyl)-4,5-dihydro-1*H-*[1,2,3]triazole* (**4a**). From 0.130 g (0.5 mmol) of **1a** and diazomethane (**3a**). Yield: 0.135 g (89%), orange oil. IR (neat): 3039, 2998, 2926, 2869, 1614, 1525, 1512, 1443, 1308, 1286, 1216, 1098, 1024, 989, 816, 704. ^{1}H-NMR: 2.35 (*s*, Me); 4.90 (br. *s*, CH_2); 7.25 (br. *s*, 4 arom. H). ^{13}C-NMR: 21.2 (Me); 70.1 (*m*, C(5)); 73.1 (C(4)); 126.9, 130.2 (4 arom. CH); 135.3, 139.4 (2 arom C_q). ESI-MS (MeOH + NaI): 320 (100, $[M + Na]^+$).

*1-(2-Methoxyphenyl)-5,5-bis(trifluoromethyl)-4,5-dihydro-1*H-*[1,2,3]triazole* (**4b**). From 0.135 g (0.5 mmol) of **1b** and **3a**. Yield: 0.120 g (80%), colorless solid; m.p. 63–65°C (hexane). IR (KBr): 3086, 3019, 2953, 2847, 1599, 1530, 1504, 1468,1439, 1308, 1284, 1226, 1208, 1181, 1104, 1025, 1003, 969, 769, 702. ^{1}H-NMR: 3.80 (*s*, MeO); 4.85 (br. *s*, CH_2); 7.00–7.40 (*m*, 4 arom. H). ^{13}C-NMR: 55.5 (MeO); 68.2 (*m*, $^2J_{CF}$ = 31 Hz, C(5)); 71.7 (C(4)); 126.4 (*q*, $^1J_{CF}$ = 252 Hz, 2 CF_3); 112.7, 120.9, 130.9, 131.7 (4 arom. CH); 125.4 (1 arom. C_q-N); 157.7 (1 arom. C_q-O). ^{19}F-NMR: –72.7 (2 CF_3). CI-MS: 315 (14), 314 (100, $[M+1]^+$), 286 (59), 285 (14). ESI-MS (MeOH + NaI): 336 (100, $[M + Na]^+$). Anal. Calc. for $C_{12}H_{11}F_6N_3O$ (327.23): C 44.05, H 3.39. Found: C 44.27, H 3.39.

*4-Methyl-1-(4-methylphenyl)-5,5-bis(trifluoromethyl)-4,5-dihydro-1*H-*[1,2,3]triazole* (**4c**). From 0.130 g (0.5 mmol) of **1a** and diazoethane (**3b**). Yield: 0.120 g (78%), yellow oil. IR (neat): 3036, 2986, 2959, 2928, 1689, 1512, 1465, 1254, 1213, 1064, 1032, 984, 942, 819, 717. ^{1}H-NMR: 1.75 (*dq*, $^3J_{HH}$ = 7.5 Hz, $^5J_{HF}$ = 2.1 Hz, MeC(4)); 2.35 (*s*, Me); 5.00 (*qq*, $^3J_{HH}$ = 7.5, $^4J_{HF}$ = 1.3, CH); 7.25 (br. *s*, 4 arom. H). ESI-MS (MeOH + NaI): 334 (100, $[M + Na]^+$).

*4-Methyl-1-(2-methoxyphenyl)-5,5-bis(trifluoromethyl)-4,5-dihydro-1*H-*[1,2,3]triazole* (**4d**). From 0.135 g (0.5 mmol) of **1b** and **3b**. Yield: 0.130 g (84%), colorless solid; m.p. 69–70°C (hexane). IR (neat): 3022, 2980, 2946, 2914, 1846, 1602, 1519, 1499, 1465, 1283, 1258, 1204, 1130, 1064, 987, 769. ^{1}H-NMR: 1.75 (*dq*, $^3J_{HH}$ = 7.5, $^5J_{HF}$ = 2.1, Me); 3.80 (*s*, MeO); 5.00 (*qq*, $^3J_{HH}$ = 7.5, $^4J_{HF}$ = 1.3, CH); 6.96–7.43 (*m*, 4 arom. H). ^{13}C-NMR: 13.5 (Me); 55.7 (MeO); 71.2 (*m*, $^2J_{CF}$ = 34 Hz, C(5)); 79.9 (C(4)); 122.0 (*q*, $^1J_{CF}$ = 290, CF_3); 122.9 (*q*, $^1J_{CF}$ = 285, CF_3); 112.3, 120.4, 130.4, 131.1 (4 arom. CH); 127.7 (1 arom. C_q-N); 157.0 (1 arom. C_q-O). ^{19}F-NMR: –71.7 (*q*, $^4J_{FF}$ = 9.9, CF_3); –66.8 (*q*, $^4J_{FF}$ = 9.0, CF_3). CI-MS: 329 (13), 328 (100, $[M+1]^+$), 300 (25), 299 (28), 122 (14). ESI-MS (MeOH + NaI): 350 (100, $[M + Na]^+$).

Suitable crystals for an X-ray crystal-structure determination were obtained from hexane.

3. Reaction of imine 2 with diazoalkanes 3. *General procedure.* To a solution of imine **2** (0.128 g, 0.5 mmol) in 3 ml of Et_2O, a three-fold excess of the respective diazo compound dissolved in Et_2O was

added at –60°C. After 6 h, the mixture was slowly warmed to room temperature. The solvent was evaporated and the crude products were purified by crystallization.

*1-(4-Chlorophenyl)-5-trichloromethyl-4,5-dihydro-1*H-*[1,2,3]triazole* (**5a**). From imine **2** and **3a**. Yield: 0.075 g (50%), colorless solid; m.p. 158–159°C (benzene/hexane). IR (KBr): 3089, 3056, 3031, 2922, 2856, 1647, 1596, 1507, 1112, 1096, 1078, 940, 823, 795, 777. ^{1}H-NMR: 4.60–4.70 (*m*, CH); 4.90–5.00 (*m*, CH_2); 7.38–7.43 (*m*, 4 arom. H). ^{13}C-NMR: 67.6 (C(5)); 72.1 (C(4)); 100.0 (CCl_3); 120.3, 129.0 (4 arom. CH); 129.0, 138.9 (2 arom. C_q). CI-MS: 302 (26), 300 (56, $[M+1]^+$), 299 (5, $M^{+\bullet}$), 298 (44), 276 (11), 274 (48), 273 (11), 272 (100), 270 (78), 152 (19). ESI-MS (MeOH + NaI): 322 (100, $[M+Na]^+$).

Suitable crystals for an X-ray crystal-structure determination were obtained from hexane/CH_2Cl_2.

*4-Methyl-1-(4-chlorophenyl)-5-trichloromethyl-4,5-dihydro-1*H-*[1,2,3]triazole* (**5b**). From imine **2** and **3b**. Yield: 0.045 g (29%), colorless solid; m.p. 108–110°C (hexane). IR (KBr): 3036, 2986, 2959, 2928, 1689, 1613, 1512, 1465, 1279, 1213, 1064, 1032, 942, 819, 717. ^{1}H-NMR: 1.45 (*d*, *J* = 7.4 Hz, Me); 4.40 (*d*, *J* = 7.4 Hz, HC(5)); 4.80–5.10 (*dq*-like, HC(4)); 7.40–7.50 (*m*, 4 arom. H). ESI-MS (MeOH + NaI): 336 (100, $[M + Na]^+$).

4. Thermal decomposition of triazoles 4a and 5a. 4.1. A neat sample of **4a** (0.09 g, 0.3 mmol) was heated to 150°C for 10 h to give *1-(4-methylphenyl)-2,2-bis(trifluoromethyl)aziridine* (**6a**). Yield: 0.03 g (37%). ^{1}H-NMR: 2.15 (*s*, Me); 2.40 (*s*, CH_2); 7.10–7.30 (*m*, 4 arom. H). ESI-MS (MeOH + NaI): 292 (100, $[M+Na]^+$). 4.2. A sample of **5a** (0.1 g, 0.3 mmol) was heated in boiling toluene for 10 h. Then, the solvent was evaporated and the residue was separated by column chromatography (SiO_2, benzene/hexane) to give *1-(4-chlorophenyl)-2-(trichloromethyl)aziridine* (**6b**). Yield: 0.04 g (44%). ^{1}H-NMR: 2.30 (*d*, *J* = 6 Hz, HC(3)); 2.80 (*d*,*J* = 2.8 Hz, HC(3)); 3.10 (*dd*,*J* = 6.0, 2.8 Hz, HC(2)); 6.90–7.20 (*m*, 4 arom. H). ESI-MS (MeOH + NaI): 293 (100, $[M + Na]^+$).

5. Attempted reactions of imines 1a and 2 with dimethoxycarbene. A solution containing 160 mg (1 mmol) of **7** and 0.5 mmol of the corresponding imine **1** or **2** in 2 ml abs. toluene was heated to reflux under an argon atmosphere. After 8 h, the decomposition of **7** was complete, and evaporation of the solvent afforded an oily residue, which was analyzed by means of ^{1}H-NMR spectroscopy. Only one signal of the MeO group located at 3.53 ppm, attributed to 1,1,2,2-tetramethoxyethene [31] (DMC dimer), was observed in the spectrum.

6. X-ray crystal-structure determination of 4d and 5a (see Table 1 and Figs. 1–2)*. All measurements were made on a *Nonius KappaCCD diffractometer* [32] using graphite-monochromated MoK_α radiation (l 0.71073 Å) and an Oxford Cryosystems Cryostream 700 cooler. Data reduction was performed with *HKL Denzo and Scalepack* [33]. The intensities were corrected for *Lorentz* and polarization effects, and in the case of **5a**, an absorption correction based on the multi-scan method [34] was applied. Equivalent reflections, other than *Friedel* pairs in **5a**, were merged. Data collection and refinement parameters are given in Table 1, and views of the molecules are shown in Figs. 1 and 2. The structures were solved by direct methods using SHELXS97 [35] for **4d** and SIR92 [36] for **5a**, which revealed the positions of all non-H-atoms. The non-H-atoms were refined anisotropically. All of the H-atoms were placed in geometrically calculated positions and refined using a riding model where each H-atom was assigned a fixed isotropic displacement parameter with a value equal to $1.2U_{eq}$ of its parent C-atom ($1.5U_{eq}$ for the Me groups of **4d**). Refinement of each structure was carried out on F^2 using full-matrix least-squares procedures, which minimized the function $\Sigma w(F_o^2 - F_c^2)^2$. A correction for secondary extinction was applied in each case. In the cases of **4d** and **5a**, four and one reflections, respectively, whose intensities were considered to be extreme outliers, were omitted from the final refinement. The space group for each compound is non-centrosymmetric, but the space group symmetry dictates that each compound is racemic. For **4d**, the absolute structure was chosen arbitrarily. For **5a**, the absolute structure was deduced by refinement of the absolute structure parameter [37], which converged at a value of 0.03(6). Neutral atom scattering factors for non-H-atoms were taken from [38a], and the scattering factors for H-atoms were taken from [39]. Anomalous dispersion effects were included in F_c [40]; the values for f' and f'' were those of [38b]. The values of the mass attenuation coefficients are those of [38c]. All calculations were performed using the SHELXL97 [41] program.

*CCDC: 618710–618711 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the *Cambridge Crystallographic Data Centre via* ww.ccdc.cam.ac.uk/data_reguest/cif.

Table 1. Crystallographic data for compounds **4d** and **5a**.

	4d	**5a**
Crystallized from	hexane	hexane/CH_2Cl_2
Empirical formula	$C_{12}H_{11}F_6N_3O$	$C_9H_7Cl_4N_3$
Formula weight [g mol^{-1}]	327.23	298.99
Crystal color, habit	colorless, prism	colorless, tablet
Crystal dimensions [mm]	0.15×0.17×0.20	0.10×0.25×0.28
Temperature [K]	160(1)	160(1)
Crystal system	orthorhombic	monoclinic
Space group	*Pna*2$_1$	*Cc*
Z	4	4
Reflections for cell determination	1763	11379
2θ range for cell determination [°]	4–55	4–60
Unit cell parameters *a* [Å]	9.7698(2)	10.2967(3)
b [Å]	17.8094(4)	19.5793(6)
c [Å]	7.5939(1)	5.8129(1)
β [°]	90	97.184(2)
V [Å^3]	1321.30(4)	1162.69(5)
D_X [g cm^{-3}]	1.645	1.708
μ(MoK_α) [mm^{-1}]	0.165	0.989
Scan type	φ and ω	φ and ω
$2\theta_{(max)}$ [°]	55	60
Transmission factors (min; max)	–	0.815; 0.908
Total reflections measured	30482	14459
Symmetry independent reflections	1616	3368
Reflections with $I>2\sigma(I)$	1458	3004
Reflections used in refinement	1612	3367
Parameters refined; restraints	202; 1	146; 2
Final *R(F)* [$I>2\sigma(I)$ reflections]	0.0355	0.0311
wR(F^2) (all data)	0.0963	0.0702
Weights:[a)] a; b	0.0572; 0.2541	0.0282; 0.8195
Goodness of fit	1.078	1.069
Secondary extinction coefficient	0.021(4)	0.0037(8)
Final Δ_{max}/σ	0.001	0.002
Δρ (max; min) [eÅ^{-3}]	0.24; –0.17	0.25; –0.27

a) $w = [\sigma^2(F_o^2) + (aP)^2 + bP]^{-1}$, where $P = (F_o^2 + 2F_c^2)/3$

Acknowledgment

G. M. thanks the *Polish State Committee for Scientific Research* (Grant PBZ-KBN-126/T09/12) for financial support. Superior technical assistance by Mrs. *M. Celeda* is also acknowledged. *H. H.* thanks *F. Hoffmann-La Roche AG*, Basel, for financial support.

REFERENCES

1. Regitz M. and Heydt H., in '*1,3-Dipolar Cycloaddition Chemistry*', Ed. Padwa A., J. Wiley & Sons, New York, 1984, Vol. 1, p. 653.
2. Maas G., in '*The Chemistry of Heterocyclic Compounds, Vol. 59: Synthetic Applications of 1,3-Dipolar Cycloadition Chemistry Toward Heterocycles and Natural Products*', Eds. Padwa A. and Pearson W.H., J. Wiley & Sons, New York, 2002, p. 539.
3. Bartnik R., Lesniak S. and Wasiak P., *Tetrahedron Lett*., **45**, 7301 (2004).
4. '*Rational Drug Design and the Discovery of the 1,2,3-Triazolines as a Unique Class of Anticonvulsants and Antiischemic Agents*', Ed. Kadaba P.K., *Curr. Med. Chem.,* **10** (2003).
5. Kadaba P.K., *Pestic. Sci.,* **42**, 299 (1994).
6. Jacquot S., Belaissaoui A., Schmitt G., Laude B., Kubicki M.M. and Blacque O., *Eur. J. Org. Chem.*, 1541 (1999).
7. Coe P.L. and Holton A.G., *J. Fluorine Chem.,* **10**, 553 (1977).
8. Bartnik R. and Mloston G., *Tetrahedron*, **40**, 2569 (1984); Bartnik R. and Mloston G., *Synthesis*, 924 (1983).
9. Rasmussen K.G. and Jørgensen K.A., *J. Chem. Soc., Perkin Trans. 1*, 1287 (1997); Rasmussen K.G., Juhl K., Hazell R.G. and Jørgensen K.A., *J. Chem. Soc., Perkin Trans. 2,* 1347 (1998).
10. Nagayama S. and Kobayashi S., *Chem. Lett*., 685 (1998).
11. Lee S.-H., Han T.-D., Yu K. and Ahn K.-H., *Bull. Korean Chem. Soc.,* **22**, 449 (2001).
12. Kubo T., Sakaguchi S. and Ishii Y., *Chem. Commun.*, 625 (2000).
13. Hansen K.B., Finney N.S. and Jacobsen E.N., *Angew. Chem., Int. Ed. Engl*., **34**, 676 (1995).
14. Patani G.A. and LaVoie E.J., *Chem. Rev.,* **96**, 3147 (1996).
15. Maienfisch P. and Hall R.G., *Chimia*, **58**, 93 (2004).
16. Zeifman Y.V., Gambarian N.P., Simonian L.A., Minasian R.B. and Knunjanc I.L.,*J. Gen. Chem. USSR,* **37**, 2355 (1967).
17. Kostyanowski R.G., Kadorkina G.K., Czerwin I.I. and Romero Maldonado I.K.A., *Chem. Heterocycl. Comp.,* 616 (1988).
18. Burger K., Thenn W., Fehn J., Gieren A. and Narayanan P., *Chem. Ber.,* **107**, 1526 (1974).
19. Belaissaoui A., Jacquot S., Morpain C., Schmitt G., Vebrel J. and Laude B., *Can. J. Chem.,* **75**, 523 (1997).
20. Ishikawa N. and Kitazume T., *Bull. Chem. Soc. Jpn.,* **46**, 3260 (2000).
21. Huisgen R. and Szeimies G., *Chem. Ber.,* **98**, 1153 (1965).
22. Johnson C.K., *ORTEP II.* Report ORNL-5138, Oak Ridge National Laboratory, Oak Ridge, Tennessee, 1976.
23. Ducray R. and Ciufolini M.A., *Angew. Chem., Int. Ed. Engl.,* **41**, 4688 (2002).
24. Danion-Bougot R., Danion D. and Francis G., *Tetrahedron Lett.,* **31**, 3739 (1990).
25. Broggini G., Garanti L., Molteni G. and Pilati T., *Tetrahedron: Asymmetry,* **12**, 1201 (2001).
26. Kostyanowski R.G., Tchervin I.I., Fomichov A.A., Samojlova Z.E., Makarov C.N., Zeifman Y.V. and Dyatkin B.L., *Tetrahedron. Lett.,* 4021 (1969).
27. Greenberg J. and Liebman J.F., '*Strained Organic Molecules'*, Academic Press, New York 1978, pp. 333–336; Kobayashi Y. and Kumadaki I., *Acc. Chem. Res*., **14**, 76 (1981).
28. Dawid M., Mloston G. and Warkentin J., *Org. Lett*., **3**, 2455 (2001); Dawid M., Mloston G. and Warkentin J., *Chem. Eur. J*., **8**, 2184 (2002); Zhou H., Mloston G. and Warkentin J., *Org. Lett*., **7**, 487 (2005); Reisenauer P., Romanski J., Mloston G. and Schreiner P.R., *Eur. J. Org. Chem.*, in press (2006).
29. El-Saidi M., Kassam K., Pole D.L., Tadey T. and Warkentin J., *J. Am. Chem. Soc*., **114**, 8751 (1992).
30. Giencke W., *Z. Naturforsch. B, Anorg. Chem. Org. Chem.*, **40**, 651 (1985).
31. Lemal D.M., Gosselink E.P. and McGregor S.D., *J. Am. Chem. Soc.*, **88**, 582 (1966).
32. Hooft R., *KappaCCD Collect Software*, Nonius BV, Delft, The Netherlands, 1999.
33. Otwinowski Z. and Minor W., in '*Methods in Enzymology*', Vol. 276, '*Macromolecular Crystallography*', Part A, Eds. Carter C.W., Jr. and Sweet R.M., Academic Press, New York, 1997, p. 307.
34. Blessing R.H., *Acta Crystallogr., Sect. A,* **51**, 33 (1995).
35. Sheldrick G.M., SHELXS97, *Program for the Solution of Crystal Structures*, University of Göttingen, Germany, 1997.

36. Altomare A., Cascarano G., Giacovazzo C., Guagliardi A., Burla M.C., Polidori G. and Camalli M., SIR92, *J. Appl. Crystallogr.*, **27**, 435 (1994).
37. a) Flack H.D. and Bernardinelli G., *Acta Crystallogr., Sect. A*, **55**, 908 (1999); b) Flack H.D. and Bernardinelli G., *J. Appl. Crystallogr.*, **33**, 1143 (2000).
38. a) Maslen E.N., Fox A.G. and O'Keefe M.A., in 'International Tables for Crystallography', Ed. Wilson A.J.C., Kluwer Academic Publishers, Dordrecht, 1992, Vol. C, Table 6.1.1.1, p. 477; b) Creagh D.C. and McAuley W.J., *ibid*., Table 4.2.6.8, p. 219; c) Creagh D.C. and Hubbell J.H., *ibid*., Table 4.2.4.3, p. 200.
39. Stewart R.F., Davidson E.R. and Simpson W.T., *J. Chem. Phys.,* **42**, 3175 (1965).
40. Ibers J.A. and Hamilton W.C., *Acta Crystallogr.*, **17**, 781 (1964).
41. Sheldrick G.M., SHELXL97, *Program for the Refinement of Crystal Structures*, University of Göttingen, Germany, 1997.